DETAILED ACTION

Acknowledgement of Receipt

Applicant's response filed on 08/24/2010 to the Office Action mailed on 05/26/2010 is acknowledged.

Claim Status

Claims 20-34 are pending.

Claims 1-19 are cancelled.

Claims 20-34 have been examined.

Claims 20-34 are rejected.

Rejections and/or objections not reiterated from the previous Office Action are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following rejection is new.

1. Claims 20-29 and 31-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Infeld et al. (International Application Published Under the PCT WO 02/089835 A2, Published 11/14/2002) in view of Babcock et al. (European Patent Application 1027886 A2, Published 08/16/2000).

The claims are directed to solid composition comprising particles of at least 5% low-solubility amorphous drug, at least 5% poloxamer, and a stabilizing polymer such as hydroxypropyl methyl cellulose acetate succinate (HPMCAS). The claims are further directed to an anti-viral drug. The claims are further directed to the amount of HPMACS being present such that the MDC of the drug is increased at least 1.25 fold over a control.

Infeld et al. show a tablet comprising a kernel having 61.3% nelfinavir mesylate, 33.1% poloxamer 188, 3.4% microcrystalline cellulose, corn starch, and magnesium stearate. (page 12, example 5). Nelfinavir mesylate is an low-soluble, amorphous, hydrophobic antiviral drug. (page 1, Lines 5-28). The drug kernel is made by melt granulation process which results in the formation of particles. (page 6, Lines 7-15). The presence of poloxamer enhances the bioavailability of the drug. (page 2, Lines 15-16).

Infeld et al. lacks a teaching wherein the particles further comprise a stabilizing polymer such as hydroxypropyl methyl cellulose acetate succinate (HPMCAS).

Babcock et al. show a solid dispersion of a low-solubility drug and a polymer. (abstract). The preferred polymer is cellulosic. (page 29, Lines 19-36). The most preferred polymer is the stabilizing polymer HPMCAS. (page 33, Lines 23-27). HPMC will stabilize amorphous low-soluble drugs so that they do not undergo change to crystalline form overtime during storage. (page 3, Lines 5-14). This dispersion provides an MCD and AUC of 1.25 fold over a control composition. (page 7, Lines 17-30).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the composition of Infeld et al. by adding HPMCAS taught by Babcock et al. to the composition. One of ordinary skill in the art would have been motivated to do so in order to provide enhanced stability to the tablet formulation of Infeld et al. With regard to the instantly claimed glass transition temperature of the particle and drug as instantly claimed, it would be expected that the particles taught by Infeld et al. as modified by Babcock et al. would also possess this property. With regard

to the instantly claimed method of making the composition, this is a product-by-process limitation that is not given patentable weight in a product claim.

The following rejection is new.

2. Claim20-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beyernick et al. (US Patent Application 2003/0163931 A1, Published 09/04/2003).

The claims are directed to solid composition comprising particles of at least 5% low-solubility amorphous drug, at least 5% poloxamer, and a stabilizing polymer such as hydroxypropyl methyl cellulose acetate succinate (HPMCAS). The claims are further directed to [2R,4S] 4-[(3,5-bis-trifluoromethyl-benzyl)-methoxy- carbonyl-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carbo-xylic acid ethyl ester. The claims are further directed to the amount of HPMACS being present such that the MDC of the drug is increased at least 1.25 fold over a control.

Beyernick et al. teach a method of making a homogeneous spray-dried solid amorphous dispersion. (title). A preferred particle comprises 25% [2R,4S] 4-[(3,5-bis-trifluoromethyl-benzyl)-methoxy-carbonyl-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carbo-xylic acid ethyl ester and 75% HPMCAS. (paragraph 0122). This dispersion provides an MCD and AUC of 1.25 fold over a control composition. (paragraph 0047). The particle can also have a blend of polymers such as HPMCAS and poloxamer. (page 19, claim 19).

Bayernick et al. does not show a particle composition that comprises poloxamer.

Infeld et al. show a tablet comprising a kernel having 61.3% nelfinavir mesylate, 33.1% poloxamer 188, 3.4% microcrystalline cellulose, corn starch, and magnesium stearate. (page 12, example 5). Nelfinavir mesylate is an low-soluble, amorphous, hydrophobic antiviral drug. (page 1, Lines 5-28). The drug kernel is made by melt granulation process which results in the formation of particles. (page 6, Lines 7-15). The presence of poloxamer enhances the bioavailability of the drug. (page 2, Lines 15-16).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the composition of Bayernick et al. by adding poloxamer as taught by Infeld et al. One would have been motivated to do so since Infeld et al. teach that the addition of poloxamer would enhance the bioavailability of the active ingredient. With regard to the instantly claimed glass transition temperature of the particle and drug as instantly claimed, it would be expected that the particles taught by Bayernick et al. as modified by Infeld et al. would also possess this property.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALI SOROUSH whose telephone number is (571)272-9925. The examiner can normally be reached on M-F (9am-6pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun G. Sajjadi can be reached on (571)272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/A. S./
Examiner, Art Unit 1617

/KARLHEINZ R SKOWRONEK/
Primary Examiner, Art Unit 1631

November 5, 2010